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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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Morey Kraus

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CLARK & ELBING LLP
101 FEDERAL STREET
BOSTON, MA 02110

EXAMINER

BARNHART, LORA ELIZABETH

ART UNIT

PAPER NUMBER

1651

NOTIFICATION DATE

DELIVERY MODE

05/14/2010

ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

patentadministrator@clarkelbing.com

Office Action Summary	Application No. 10/583,684	Applicant(s) KRAUS ET AL.	
	Examiner Lora E. Barnhart	Art Unit 1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 18 February 2010.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-18 and 33-47 is/are pending in the application.
- 4a) Of the above claim(s) 2-4,6,8-18 and 33-47 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1,5 and 7 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date <u>4/5/07</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Claims 1-18 and 33-47 as recited in the 6/19/06 listing are currently pending.

Election/Restrictions

Applicant's election without traverse of Group I, claims 1-8, in the reply filed on 2/18/10 is acknowledged. Applicant's election without traverse of the species "pancreatic disease" in the same reply is further acknowledged.

Claims 9-18 and 33-47 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Claims 2-4, 6, and 8 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected species, there being no allowable generic or linking claim.

Examination on the merits will commence at this time on claims 1, 5, and 7 ONLY, to the extent they read on the elected species where applicable.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 5, and 7 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treating a pancreatic disease by administering

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a progeny cell that is a pancreatic cell to a patient with a pancreatic disease, does not reasonably provide enablement for treating any pancreatic disease by administering the pluripotent cell described in claim 1 or by administering any non-pancreatic progeny cell. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The factors to be considered in determining whether undue experimentation is required are summarized in *In re Wands*, 858 F.2d 731, 737, 8 USPQd 1400, 1404 (Fed. Cir. 1988) (a) the breadth of the claims; (b) the nature of the invention; (c) the state of the prior art; (d) the level of one of ordinary skill; (e) the level of predictability in the art; (f) the amount of direction provided by the inventor; (g) the existence of working examples; and (h) the quantity of experimentation needed to make or use the invention based on the content of the disclosure. While all of these factors are considered, a sufficient number are discussed below so as to create a *prima facie* case.

In light of the species election, claim 1 is drawn to a method of treating a (i.e., any) pancreatic disease (presumably, in a patient affected with such a disease; see below) by administering either a "pluripotent cell" having particular properties or a "progeny cell" derived from that pluripotent cell. These elements will be addressed in turn.

The specification is not enabling for treating all pancreatic conditions.

The specification provides no particular limitation on the term "pancreatic disease," so the examiner has afforded it its plain-language definition, i.e. any disease

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of or involving the pancreas. The scope of these diseases is broad and diverse, including not only the canonical pancreatic disease diabetes mellitus types I and II, but also pancreatic cancer, insulin resistance, pancreatic sepsis, pancreatitis (both acute and chronic), bile duct cysts, and pancreatic fistula, to name a few. At least some of these diseases had no effective treatment at the time of the invention; in particular, pancreatic cancer is well known as one of the most aggressive and least-treatable cancers. Hidalgo (2010, *New England Journal of Medicine* 362: 1605-1617; reference U), writing years after the invention, teaches that less than 5% of pancreatic cancer patients survive beyond 5 years. See page 1605. Hidalgo concludes that there is "much room for improvement in all aspects of treatment for pancreatic cancer." See page 1615. Pezzilli et al. (2006, *Journal of Pancreas Online* 7: 79-91; reference V), also writing years after the invention, teaches that acute pancreatitis is only treatable during a narrow window of time. See page 80. Pezzilli teaches that the effective treatment of this condition was complicated, even after the invention was made. See, e.g., page 87 (discussing the positive and negative aspects of treating pancreatitis with prophylactic antibiotics). Overall, the treatment of "pancreatic disease" as a genus was unpredictable at the time of the invention.

M.P.E.P. § 2164.03 reads, "The amount of guidance or direction needed to enable the invention is inversely related to the amount of knowledge in the state of the art as well as the predictability in the art. *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). The 'amount of guidance or direction' refers to that information in the application, as originally filed, that teaches exactly how to make or use the invention.

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The more that is known in the prior art about the nature of the invention, how to make, and how to use the invention, and the more predictable the art is, the less information needs to be explicitly stated in the specification. **In contrast, if little is known in the prior art about the nature of the invention and the art is unpredictable, the specification would need more detail as to how to make and use the invention in order to be enabling.** See, e.g., *Chiron Corp. v. Genentech Inc.*, 363 F.3d 1247, 1254, 70 USPQ2d 1321, 1326 (Fed. Cir. 2004)...In applications directed to inventions in arts where the results are unpredictable, the disclosure of a single species usually does not provide an adequate basis to support generic claims. In cases involving unpredictable factors, such as most chemical reactions and physiological activity, more may be required.” As the above discussion illustrates, treating at least a few pancreatic diseases was unpredictable at the time of the invention, so this treatment must be considered “nascent,” and the amount of guidance required is relatively high.

The instant specification provides no particular guidance for treating each and every pancreatic disease with any cell or active agent. The working examples include none in which any cells are administered to any patient with a pancreatic disease. The only possibly relevant examples, Examples 6-8 at pages 26-27, are limited to what appear to be prophetic administrations of stem cells into hepatectomized mice or preimmune sheep. These examples provide insufficient guidance to practice the invention, considering its unpredictable nature.

The specification is not enabling for treating any pancreatic diseases by administering the “pluripotent cells” in claim 1.

The examiner has established the nascent nature of the pancreatic disease treatment art. Claim 1 is drawn in part to administering "pluripotent cells," which the specification indicates can be used interchangeably with "stem cells," to a patient with a pancreatic disease to treat that disease. See page 6, lines 13-15. As discussed above, however, the only working examples that could possibly be considered relevant to the claimed treatment method of Examples 6-8, and none of these prophetic examples appear to treat a pancreatic disease. These examples provide insufficient guidance to practice the invention, considering its unpredictable nature.

The specification is not enabling for treating any pancreatic diseases by administering any "progeny cells" other than pancreatic cells per se

The examiner has established the nascent nature of the pancreatic disease treatment art. Claim 1 is drawn in part to administering "progeny cells derived from pluripotent cells" to a patient with a pancreatic disease to treat that disease. As discussed above, however, the only working examples that could possibly be considered relevant to the claimed treatment method of Examples 6-8, and none of these prophetic examples appear to treat a pancreatic disease. These examples provide insufficient guidance to practice the invention, considering its unpredictable nature. The term "progeny cell derived from a pluripotent cell" is broad and includes all possible progeny cell types, not just those that might be reasonably expected to treat the disease of interest. None of the working examples show that administering liver cells, for example, could treat a pancreatic disease.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

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The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 5, and 7 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is drawn to “a method of treating a pancreatic disease . . . comprising the step of administering to a patient [a cell],” which is confusing because the claim does not particularly require that the patient being administered the cell be afflicted with the disease. Clarification is required.

Claim 1 refers to “a pluripotent cell” that expresses certain markers and has certain capacities; the specification describes this cell at page 6, lines 13-15, as being “interchangeable” in meaning with “stem cell.” However, this definition is repugnant to the art, which considers “pluripotent cells” to be not just able to give rise to “two or more cell types of an organism” (i.e. “multipotent”), but to be able to give rise to all cell types within an organism. Embryonic stem cells are pluripotent; see Donehower et al. (1996, U.S. Patent 5,569,824; reference A; at column 3, line 57, through column 4, line 8).

An applicant is entitled to be his or her own lexicographer and may rebut the presumption that claim terms are to be given their ordinary and customary meaning by clearly setting forth a definition of the term that is different from its ordinary and customary meaning(s). See *In re Paulsen*, 30 F.3d 1475, 1480, 31 USPQ2d 1671, 1674 (Fed. Cir. 1994), quoting *Intellicall, Inc. v. Phonometrics, Inc.*, 952 F.2d 1384, 1387-88, 21 USPQ2d 1383, 1386 (Fed. Cir. 1992). Any special meaning assigned to a term “must be sufficiently clear in the specification that any departure from common usage would

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be so understood by a person of experience in the field of the invention.” *Multiform Desiccants Inc. v. Medzam Ltd.*, 133 F.3d 1473, 1477, 45 USPQ2d 1429, 1432 (Fed. Cir. 1998). Consistent with the well-established axiom in patent law that a patentee or applicant is free to be his or her own lexicographer, a patentee or applicant may use terms in a manner contrary to or inconsistent with one or more of their ordinary meanings if the written description clearly redefines the terms. See, e.g., *Process Control Corp. v. HydReclaim Corp.*, 190 F.3d 1350, 1357, 52 USPQ2d 1029, 1033 (Fed. Cir. 1999). Accordingly, when there is more than one definition for a term, **it is incumbent upon applicant to make clear which definition is being relied upon to claim the invention.** Until the meaning of a term or phrase used in a claim is clear, a rejection under 35 U.S.C. 112, second paragraph is appropriate. In applying the prior art, the claims should be construed to encompass all definitions that are consistent with applicant’s use of the term. See *Tex. Digital Sys., Inc. v. Telegenix, Inc.*, 308 F.3d 1193, 1202, 64 USPQ2d 1812, 1818 (Fed. Cir. 2002). See M.P.E.P. §§ 2111.01 and 2173.05(a).

Here, applicant has not adequately limited “pluripotent cell.” The specification equates it with “stem cell,” which includes both pluripotent ES cells and multipotent mesenchymal stem cells (i.e., the cells with the expression pattern in elements (a) and (b) of claim 1); see page 6. However, the specification also refers to “a number of types of mammalian pluripotent cells,” including among them multipotent mesenchymal stem cells and pluripotent ES cells. See page 1, lines 10-25. It is not clear whether applicant intends “pluripotent” to have its accepted meaning or the contrary one. Clarification is

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required. The examiner suggests applicant replace “pluripotent cell” with “stem cell” wherever it occurs in claim 1.

Claim 1 refers to “a progeny cell derived [from a pluripotent cell],” which is indefinite because the term “derived” does not place any useful limit on the degree of similarity between the pluripotent cell and the progeny cell. Cells “derived from” pluripotent cells can include cell types that differentiate from the pluripotent cell *in vitro* or *in vivo*; cells yielded by transfecting pluripotent cells with DNA constructs; cells yielded by immortalizing pluripotent cells with virus; cells arising from embryos growing from pluripotent cells implanted into recipients, and so on. It is not clear how closely related a progeny cell must be to a pluripotent cell to be considered “derived from” it. Clarification is required.

Claim 1 requires that the cell be “capable of” differentiating into any of various cell types, but it is not clear whether this differentiation is necessarily part of the claimed method or whether it merely describes an ability that the cells have under some unnamed conditions. Clarification is required.

Because claims 5 and 7 depend from indefinite claim 1 and do not clarify the point of confusion, they must also be rejected under 35 U.S.C. 112, second paragraph.

Claim 7 requires that the method comprise “administering said cell to effect organ regeneration,” but it is not clear whether this regeneration actually occurs as part of the method or whether this limitation merely recites one possible intended use of the administration step. Clarification is required.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 5, and 7 are rejected under 35 U.S.C. 102(b) as being anticipated by Shapiro et al. (2000, *New England Journal of Medicine* 243: 230-238; on 4/5/07 IDS). This rejection is drawn to the embodiment in which the pancreatic disease is type 1 diabetes mellitus and the progeny cell is a pancreatic islet.

Shapiro teaches transplanting pancreatic islets into patients with type 1 diabetes mellitus. See page 231. Shapiro teaches that patients so treated have decreased need for exogenous insulin. See page 235.

The limitation “a progeny cell derived [from a pluripotent cell having certain properties] is a product-by-process limitation. M.P.E.P. § 2113 reads, “Product-by-process claims are not limited to the manipulations of the recited steps, only the structure implied by the steps.”

“Even though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process.” *In re Thorpe*, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985) (citations omitted).

The structure implied by the process steps should be considered when assessing the patentability of product-by-process claims over the prior art, especially where the product can only be defined by the process steps by which the product is made, or where the manufacturing process steps would be expected to impart distinctive structural characteristics to the final product. See, e.g., *In re Garnero*, 412 F.2d 276, 279, 162 USPQ 221, 223 (CCPA 1979)

The use of 35 U.S.C. §§ 102 and 103 rejections for product-by-process claims has been approved by the courts. “[T]he lack of physical description in a product-by-process claim makes determination of the patentability of the claim more difficult, since in spite of the fact that the claim may recite only process limitations, it is the patentability of the product claimed and not of the recited process steps which must be established. We are therefore of the opinion that when the prior art discloses a product which reasonably appears to be either identical with or only slightly different than a product claimed in a product-by-process claim, a rejection based alternatively on either section 102 or section 103 of the statute is eminently fair and acceptable. As a practical matter, the Patent Office is not equipped to manufacture products by the myriad of processes put before it and then obtain prior art products and make physical comparisons therewith.” *In re Brown*, 459 F.2d 531, 535, 173 USPQ 685, 688 (CCPA 1972).

Once a product appearing to be substantially identical is found and an art rejection made, the burden shifts to the applicant to show an unobvious difference. In this case, applicant could overcome this rejection by showing that the manner in which pancreatic islets are prepared has an effect on the claimed method. Until this fact is

established by evidence, islets obtained directly from a pancreas (as were Shapiro's) will be considered identical to islets derived from the pluripotent cells recited in claim 1.

No claims are allowed. No claims are free of the art.

Applicant is requested to specifically point out the support for any amendments made to the disclosure in response to this Office action, including the claims (MPEP 714.02 and 2163.06). In doing so, applicant is requested to refer to pages and line numbers in the as-filed specification, **not** the published application. Due to the procedure outlined in MPEP § 2163.06 for interpreting claims, it is noted that other art may be applicable under 35 U.S.C. § 102 or 35 U.S.C. § 103(a) once the aforementioned issue(s) is/are addressed.

Applicant is requested to provide a list of all copending U.S. applications that set forth similar subject matter to the present claims and share an inventor or assignee with the instant application. A copy of such copending claims is requested in response to this Office action in order to assist the examiner with double patenting analysis in the application.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lora E. Barnhart whose telephone number is 571-272-1928. The examiner can normally be reached on Monday-Thursday, 9:00am - 5:30pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael G. Wityshyn can be reached on 571-272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Lora E Barnhart/
Primary Examiner, Art Unit 1651